

### **REMARKS**

In an Office Action dated April 15, 2004, claims 15-16, 18-19, 23-24, 28-41, 43-45, and 84-89 in the subject patent application were rejected. Claims 46-83 and 96-98 in the application were objected to and claims 25, 27, 42, and 90-95 were allowed. By amendment above, claims 19, 28, 43, 46, 84, and 89 have been rewritten. Support for the amendments to claims 19 and 84 can be found in claims 19 and 84 as previously presented and in claim 15 as previously presented. Support for the amendments to claims 28 and 43 can be found on page 4 of the specification. Support for the amendments to claim 46 can be found in claims 43 and 46 as previously presented. Support for the amendments to claim 89 can be found in claim 89 as previously presented.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

The Examiner has rejected claims 19 and 84-88 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Examiner claims 19 and 88 (we assume the Examiner meant claim 84) define  $X^1$  to be  $NR^3R^4$ ,  $OR^3$ , etc. It is the Examiner's position that in doing so the valance of the organic groups are not satisfied, because both  $R^3$  and  $R^4$  could be H. In addition, the Examiner asserts that the term "any organic radical" in  $R^3$  is very broad rendering the claim indefinite.

Applicants submit that in claims 19 and 84  $X^1$  as claimed represents the residue of  $NR^3R^4$ ,  $OR^3$ ,  $SR^3$ ,  $COOR^3$ ,  $CONR^3R^4$ , or  $COR^5$  as the result of the reaction of one monomer with

a second monomer. In each monomer the  $R^3$ ,  $R^4$  or  $R^5$  substituents are the reactive substituents in a reaction with the second monomer as is clearly disclosed in the specification. Therefore, the valency of the organic groups in the compounds claimed is satisfied. Furthermore, applicants amended claims 19 and 84 to reflect the arrangement described above more clearly. Claims 19 and 84, as amended, recite in part “in which  $X^1$  is in each case independently the reaction residue of  $NR^3R^4$ ,  $OR^3$ ,  $SR^3$ ,  $COOR^3$ ,  $CONR^3R^4$ , or  $COR^5$  as a result of the reaction of a first monomer with a second monomer to form the dimer of formula IV”. Thus, in claims 19 and 84, as amended, the valency of the organic groups is satisfied. In addition applicants have amended claims 19 and 84 to replace  $-CH-X^1-X^1-CH-$  with  $-CH_2-X^1-X^1-CH_2-$  in the formula to more clearly define the subject matter of the invention, while maintaining the proper valency of the organic groups in the compounds claimed. With respect to the rejection of the term “any organic radical” applicants submit that this term in the claims is clearly defined by the specification. On page 5 and 6 of the specification the organic radicals which applicants regard as part of the invention are clearly defined. Further, applicants have noted that  $R^5$  inadvertently is not defined in claims 19 and 84. Applicants have amended claims 19 and 84 incorporating in these claims  $R^5$  as defined in claim 15. This definition of  $R^5$  in claims 19 and 84 was inadvertently omitted when claims were copied and amended in the previous communication by applicants. However, no new matter is added as  $R^5$  was already defined in claim 15 and the specification. Therefore, claims 19 and 84-88, as amended, are more clearly defined and withdrawal of the rejection is respectfully requested.

The Examiner has also rejected claim 89 under 35 U.S.C. §102(e) as anticipated by Honda et al (US 6,534,546). The Examiner asserts that compound 36 disclosed in Honda et al in

column 31 anticipates the instant pharmaceutical composition.

The compounds of claim 89, as amended are substantially different from the compounds in Honda et al. In claim 89, as amended, the substituent at R<sup>3</sup> cannot be a hydrogen. In contrast, the compounds disclosed by Honda et al have a hydrogen at the R<sup>3</sup> position. The claimed pharmaceutical composition in claim 89 is therefore distinct from Honda et al. Applicants submit that for this reason claim 89 is not anticipated by Honda et al. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner has also rejected claims 15-16, 18, 23-24, 28-41, and 43-45 under 35 U.S.C. §103(a) as being unpatentable over Honda et al. According to the Examiner Honda et al teaches structurally similar compounds and compositions as claimed in the present application. The Examiner asserts these difference between the reference and the presently claimed compounds and compositions is that the reference has not made compounds having guanidine in the para position to the alkylene amino group on the ring. According to the Examiner it would have been obvious to obtain the compounds within the generic disclosure of the reference because of their structural similarity with the claimed compounds with a reasonable expectation of achieving a successful pharmaceutical composition for treating cardiovascular diseases, absent evidence to the contrary. Applicants have assumed the Examiner meant treating cancer as opposed to cardiovascular diseases. Further, the Examiner asserts that a kit containing two or more pharmaceutical compositions is old in the art.

Applicants submit that the claims 15-16, 18, 23-24, 28-41, and 43-45 are non-obvious over Honda et al as the compositions of these claims exhibited unexpected results as is evidenced by the declaration of one of the inventors. The declaration shows that unexpectedly para

substituted compounds according to the claimed invention have inhibitory activity on uPA, whereas the same compounds being meta substituted were negative in tests for inhibitory action on uPA. In addition, claims 28 and 43, as amended also claim that the substituents X<sup>1</sup> and -NHC(NH)NH<sub>2</sub> are in the para position. Therefore, the compositions in claims 15, 28, and 43 and those dependent thereon unexpectedly have inhibitory action on uPA, because in these compositions the above identified substituents are in the para position. This inhibitory action on uPA is not taught or suggested by Honda et al. In addition, applicants note that claims 28 and 29 were previously allowed by the Examiner. No amendments have been made to these claims and the Examiner has not cited any new art which the Examiner did not use in prior Office Action rejecting other claims. Therefore, applicants submit that because the para substituted compounds according to the invention have unexpected inhibitory activity on uPA not taught or suggested by Honda et al, claims 15-16, 18, 23-24, 28-41, and 43-45 are non-obvious over Honda et al. Accordingly, withdrawal of the rejection is respectfully requested.

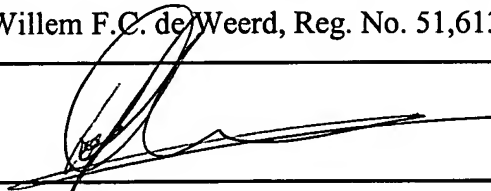
The Examiner also objected to claims 46-83, and 96-98 for being dependent upon a rejected base claim. The Examiner indicated that these claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants submit that the above arguments and amendments have overcome the Examiner's rejections of the base claims from which claims 46-83 and 96-98 are dependent. However, applicants have rewritten claims 46-83, and 96-98 in independent form as suggested by the Examiner. Accordingly, applicants respectfully request withdrawal of the Examiner's objection.

Finally, the Examiner stated that he has assumed that the subject matter of the various claims was commonly owned. Applicants confirm that the Examiner's assumption on this point is correct.

Applicants submit that the present application is now in condition for allowance.

Reconsideration and favorable action are earnestly requested.

RESPECTFULLY SUBMITTED,			
NAME AND REG. NUMBER	Willem F.C. de Weerd, Reg. No. 51,613		
SIGNATURE		DATE	7/15/64
Address	Rothwell, Figg, Ernst & Manbeck 1425 K Street, N.W., Suite 800		
City	Washington	State	D.C.
Country	U.S.A.	Teleph one	202-783-6040